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Multiple painful plaques and the Sweet's syndrome

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ABSTRACT

We present a rare case of Sweet's syndrome. A 39-year-old woman with subjective fevers, polyarthralgia, and malaise presented with worsening painful erythematous plaques on the trunk, arms, and legs. Further examination with biopsy revealed a diagnosis of acute febrile neutrophilic dermatosis, or Sweet's syndrome. Diagnosis by skin biopsy is crucial, and onset requires prompt evaluation for serious associated disorders such as leukemias, inflammatory bowel disease, thyroid disease, sarcoidosis, and infectious etiologies. In general, symptoms and cutaneous manifestations of Sweet syndrome respond rapidly to treatment with systemic corticosteroids or potassium iodide.

KEYWORDS Acute febrile neutrophilic dermatosis; classical Sweet's syndrome; Sweet's syndrome

Acute febrile neutrophilic dermatosis, also known as Sweet's syndrome (SS), traditionally manifests as acute onset fever, neutrophilia, and painful cutaneous lesions. These lesions appear as purple-red papules and plaques that are often distributed asymmetrically across the face, neck, and upper extremities. SS is characterized histologically by a diffuse infiltrate predominantly composed of mature neutrophils in the dermis. It is a rare inflammatory skin disease of unknown origin, associated with a multitude of diseases, infections, malignancies, and medications.

CASE REPORT

A 39-year-old woman from New Mexico presented with a 6-month history of a worsening painful rash on her neck, trunk, and extremities. She endorsed polyarthralgia, subjective fevers, malaise, and mild chronic dyspnea but was otherwise healthy. She denied a history of coughing, hemoptysis, conjunctivitis, diarrhea, weight loss, recent travel, or new vaccinations and medication use. Physical examination revealed several 30 to 200 mm, erythematous, indurated annular plaques on the neck, trunk, arms, and legs *(Figure 1a, 1b)*. There was no ocular, oral, or urogenital involvement and no lymphadenopathy. Further evaluation to rule out infectious, hematologic, and malignant causes included ordering a chest x-ray and tests for *Coccidioides* antibody, *Aspergillus fumigatus* IgG and IgE, urine *Histoplasma* antigen, QuantiFERON-Gold, HIV, hepatitis panel, antistreptolysin O titer, antinuclear antibody, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP), all of which were negative, with the exception of an elevated ESR and CRP. Complete blood count, renal panel, and urinalysis were within normal limits.

A biopsy specimen was obtained from a plaque on the patient's thigh. Histopathologic examination revealed a dense infiltrate of neutrophils filling the superficial dermis, papillary dermal edema, and a few eosinophils and lymphocytes *(Figure 1c)*, with no findings of vasculitis, epidermal atrophy, or mucin deposition. A diagnosis of SS was made. The patient was previously taking systemic corticosteroids for several months, but treatment was discontinued due to ocular side effects. After testing for glucose-6-phosphate dehydrogenase enzyme levels, she was transitioned to oral dapsone, 25 mg daily, and had resolution at 1-month follow-up.

DISCUSSION

SS has three subtypes: classical (idiopathic) SS, malignancy-associated SS (MASS), and drug-induced SS *(Table 1)*.[1] Classical SS is the most common type and is usually associated with infectious etiologies, autoimmune conditions, and pregnancy. SS in pregnancy typically occurs in the first or second trimester and may resolve without treatment. Lesions can recur in subsequent pregnancies, as elevated estrogen is believed to play a role in the pathogenesis of this

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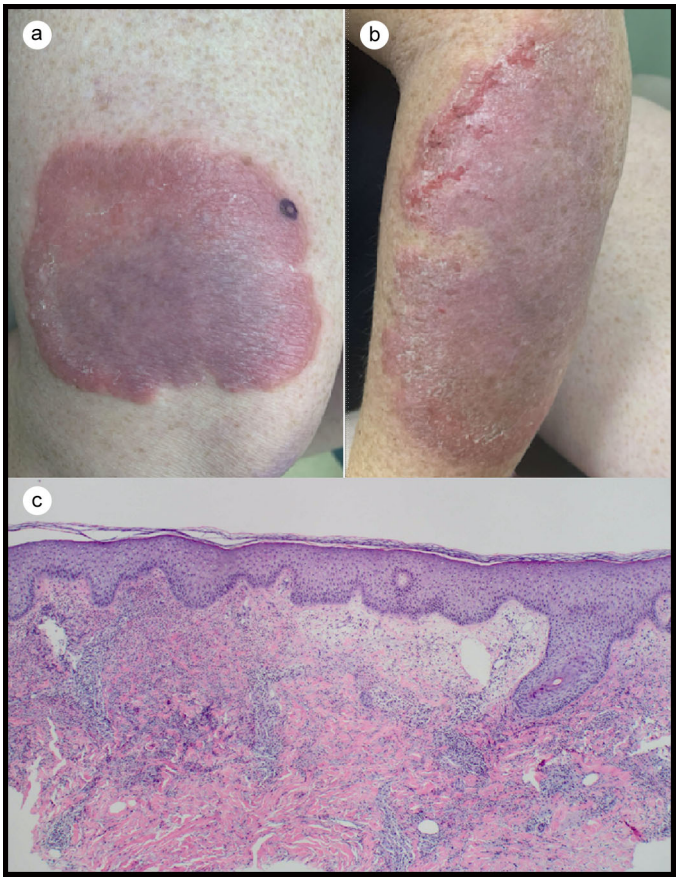

Figure 1. (a, b) Clinical photographs of several 30 to 200 mm, erythematous, indurated annular plaques on the trunk, arms, and legs. **(c)** Histopathologic findings reveal a dense infiltrate of neutrophils filling the superficial dermis, papillary dermal edema, and a few eosinophils and lymphocytes.

Table 1. Common subtypes of Sweet's syndrome and associated diseases and medications

Subtype	Associated diseases and medications
Classical	Infections
	Upper respiratory tract and gastrointestinal tract
	Autoimmune
	Inflammatory bowel disease
	Sarcoidosis
	Thyroid disease
	Pregnancy
Malignancy-associated	Hematological malignancies
	Acute myelogenous leukemia
	Solid tumors
	Genitourinary, breast, and gastrointestinal tract carcinomas
Drug-induced	Antibiotics
	Minocycline
	Nitrofurantoin
	Trimethoprim-sulfamethoxazole
	Colony-stimulating factors
	Granulocyte colony-stimulating factor
	Granulocyte-macrophage colony-stimulating factor
	Retinoids
	All-*trans*-retinoic acid
	Oral contraceptives
	Vaccines
	Bacillus Calmette-Guérin
	Smallpox
	Pneumococcal
	Influenza

Table 2. Diagnostic criteria for Sweet's syndrome*

Type	Criteria
Major criteria	1. Abrupt onset of painful erythematous plaques or nodules that may occur with vesicles, pustules, or blisters
	2. Predominantly neutrophilic dermal infiltrate without leukocytoclastic vasculitis
Minor criteria	1. Preceded by a nonspecific infection or vaccination or associated with
	a. Inflammatory diseases like chronic autoimmune disorders or infection
	b. Hemoproliferative disorders or solid malignant tumors
	c. Pregnancy
	2. Pyrexia >38°C
	3. Abnormal laboratory values (three of four)
	a. Erythrocyte sedimentation rate > 20 mm/h
	b. Elevated C-reactive protein levels
	c. Leukocytosis > 8000
	d. Neutrophilia > 70%
	4. Improvement with systemic corticosteroids or potassium iodide treatment

*Based on von den Driesch.[5,6]

subset.[2] The most common cause of MASS is acute myelogenous leukemia; however, carcinomas of the genitourinary tract, breast, and gastrointestinal tract may also be associated.[1,3] Pharmacologic agents implicated in drug-induced SS include certain antibiotics, colony-stimulating factors, retinoids, oral contraceptives, and vaccines.[1,4]

A diagnosis of SS requires the presence of both major criteria and two of the four minor criteria *(Table 2)*. Abrupt onset of painful erythematous plaques or nodules and evidence of a dense neutrophilic infiltrate without evidence of leukocytoclastic vasculitis on histopathology are the major criteria. The minor criteria include fever of ≥38°C; association with an underlying inflammatory disease, malignancy, pregnancy, or previous infection or vaccination; response to treatment of systemic corticosteroids or potassium iodide; and abnormal laboratory values (three of four) of ESR >20 mm/h, positive CRP, >8000 leukocytes, and >70% neutrophils. Our case met von den Driesch's diagnostic criteria for SS.[5,6]

The clinical presentation of SS can mimic many other systemic disorders, including lupus erythematosus and dermatomyositis; reactive erythemas like erythema multiforme and nodosum; and infectious conditions like cellulitis, erysipelas, and lymphangitis. Histologically, the differential diagnosis includes conditions with neutrophilic dermatosis such as abscesses, leukemia cutis, and pyoderma gangrenosum,

among others.[1,7] Although biopsy may reveal a diffuse infiltrate of neutrophils, this is not a confirmative finding. Therefore, it may be helpful to culture the tissue for bacterial, fungal, mycobacterial, and viral pathogens.[1]

In general, symptoms and cutaneous manifestations of SS respond rapidly to systemic corticosteroids. Other first-line agents include potassium iodide and colchicine. Second-line agents like dapsone, clofazimine, indomethacin, and cyclosporine have also proven to be effective, primarily in recurrent SS.[1,8,9] Symptomatic pregnant patients can receive a short course of systemic corticosteroids without any risk of harm to the fetus.[10] Patients should be followed shortly after beginning treatment to monitor progress. Recurrence or changes in morphology of the lesions should prompt further evaluation. Recurrence of SS is variable, but is more common in cancer patients. These patients should undergo further evaluation, as reappearance of the lesions may signify a paraneoplastic syndrome and return of malignancy.[11]

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